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10/589,811	06/08/2007	Mark L Greene	UPN-5240	2423

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EXAMINER	
TUNG, JOYCE	
ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,811	GREENE ET AL.	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *10-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/26/08,2/27/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed 8/13/09 to the Office action has been entered. Claims 1-27 are pending.

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-9 in the reply filed on 8/13/09 is acknowledged.

2. Claims 10-27 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 8/13/09.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-9 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 7,524,628, issued Apr. 28, 2009. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims 1-9 are drawn to a method for detecting molecules expressing a selected epitope in a sample comprising the steps as recited in claims 1-11 of U.S. Patent No. 7,524,628. The differences are that in the instant claim 1, a molecule expressing a selected epitope is immobilized by a biotinylated monoclonal antibody while claim 1 of U.S. Patent No. 7,524,628 requires an epitope anchor to immobilize the molecule expressing a selected epitope. As disclosed in 7,524,628, the epitope anchor comprises an antibody or other ligand or chemical specific for a selected epitope (see column 3, lines 18-21). The instant claims and claims 1-11 of U.S. Patent No. 7,524,628, issued Apr. 28, 2009 have overlapping subject matter. An obviousness-type double patenting rejection is applicable.

5. Claims 1-9 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 7,045,286, issued May 16, 2006 in view of Eberwine et al. (5,922,553, issued Jul. 13, 1999).

Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims 1-9 are drawn to a method for detecting molecules expressing a selected epitope in a sample comprising the steps as recited in claims 1-16 of U.S. Patent No.7,045,286. The differences are that claims 1-16 of U.S. Patent No. 7,045,286 require a step of adding the amplified oligonucleotide of said epitope detector from step (c) to a reverse transcriptase-based reaction or a replicase-based reaction to increase sensitivity. This step is not required by the instant claims. Eberwine et al. disclose that a first strand synthesis proceeds with

the addition of AMV-reverse transcriptase and a second strand cDNA is synthesized by T4 DNA polymerase with additional step (See column 4, lines 50-51). Thus the instant claims 1-9 are obvious over claims 1-16 of U.S. Patent No. 7,045,286. An obviousness-type double patenting rejection is applicable.

6. Claims 1-9 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 4-6, 8-12, 14-16, 18-24 of U.S. Patent No.7,361,464, issued Apr. 22, 2008.

Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims 1-9 are drawn to a method for detecting molecules expressing a selected epitope in a sample comprising the steps as recited in claims 1-2, 4-6, 8-12, 14-16, 18-24 of U.S. Patent No.7,361,464. The differences are that instant claim 1 recites the molecule which binds to the selected epitope as listed in step (b), while claim 1 of U.S. Patent No.7,361,464, recites that the epitope detector which binds to the selected epitope is selected from the group consisting of a single chain Fv and a constrained epitope selected specific CDR (see claim 1 of U.S. Patent No.7,361,464). The single chain Fv and the constrained epitope selected specific CDR are also required in the instant claims. The instant claims and claims 1-2, 4-6, 8-12, 14-16, 18-24 of U.S. Patent No.7,361,464 are related as genus-species. An obviousness-type double patenting rejection is applicable.

7. Claims 1-9 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 5-7, 9, 11-14, 16-18, 20, 22-24 of U.S. Patent No. 7,341,831, issued Mar. 11, 2008.

Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims 1-9 are drawn to a method for detecting molecules expressing a selected epitope in a sample comprising the steps claims 1-3, 5-7, 9, 11-14, 16-18, 20, 22-24 of U.S. Patent No. 7,341,831. The differences are that the molecule which binds to the selected epitope as listed in step (b) of instant claim 1 includes constrained epitope specific CDR which is comprised in an epitope detector as recited in claim 1 of U.S. Patent No. 7,341,831. The instant claims and claims 1-3, 5-7, 9, 11-14, 16-18, 20, 22-24 of U.S. Patent No. 7341831 are related as genus-species. An obviousness-type double patenting rejection is applicable.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-3 and 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eberwine et al. (5,922,553, issued Jul. 13, 1999) in view of Eberwine (7,115,371, issued Oct. 3, 2006), Waggoner (5,627,027, May 6, 1997), and Sano et al. (5,665,539, issued Sep. 9, 1997).

Eberwine et al. ('553). disclose a method, which is for detecting a selected protein by immuno aRNA (See column, 2, lines, 37-50). The presence and quantity of labeled RNA transcript is indicative of the amount of selected protein present (See column 4, lines 33-36 and columns 7-8, claims 1-2). In the method, a first antibody targeted to the selected protein is immobilized to a solid support. A RNA-promoter driven cDNA sequence is covalently coupled to a second antibody, which binds to the selected protein (See column 2, lines 37-51). The cDNA is double stranded (See column 5, lines 34-35) for use as a template for T7 RNA polymerase (see column 4, lines 41-42). The technique of a RNA synthesis is explicitly disclosed (See column 3, lines 9-24). First strand synthesis proceeds with the addition of AMV-reverse transcriptase (See column 4, lines 50-51). The solid support can be microtiter plates and beads (see column 4, lines 17-20).

Eberwine et al ('553) do not disclose a monoclonal antibody which binds to a selected epitope comprising a universal epitope.

Eberwine et al. ('371) disclose a method for detecting molecules expressing a selected epitope in a sample (see column 2, lines 47-49). The method applies a single chain Fv or CDR which contains a universal epitope such as hemagglutinin HA tag or polyhistidine tag (see column 8, lines 64-67). A single monoclonal antibody or single chain Fv coupled with a ds-DNA is the epitope detector. The efficacy of a universal epitope detector is demonstrated. After T7

polymerase amplification, specific bands from lysates of 10^{-6} dilution are detected (see column 9, lines 1-12).

One of ordinary skill in the art would have been motivated to apply a monoclonal antibody which binds to a selected epitope comprising a universal epitope as taught by Eberwine et al. ('371) because the efficiency for detection is increased (see column 9, lines 1-12). It would have been prima facie obvious to apply a monoclonal antibody which binds to a selected epitope comprising a universal epitope.

The above-cited references do not disclose the step (d) of claim 1 of contacting an amplified oligonucleotide with a fluorescence dye which stains RNA amplification product.

Waggoner discloses that cyanine dye can be used to attach to fragments of DNA or RNA to identify the presence and quantity of a specific nucleotide sequence in samples of DNA or RNA (See column 8, lines 51-56).

One of ordinary skill in the art at the time of the instant invention would have been motivated to apply a fluorescent dye, such as cyanine dye to stain unlabeled amplified RNA of Eberwine et al. for detecting and/or quantifying molecules expressing a selected epitope in a sample because as indicated by Waggoner, cyanine dye is a highly light-absorbing dye for use with nucleic acids and can be used for detection and quantification in very low amounts (See column 4, lines 35-45) It would have been prima facie obvious to apply cyanine dye for detecting or quantifying molecules expressing a selected epitope in a sample.

None of the references above discloses a biotinylated monoclonal antibody and a biotinylated oligonucleotide which form antibody and oligonucleotide complex via streptavidin.

Sano et al. disclose a linker which is a biotinylated nucleic acid marker cross-linked to biotinylated antibody by streptavidin or avidin (see column 4, lines 27-31).

One of ordinary skill in the art would have been motivated to apply the linker as taught by Sano et al. because the method of Sano et al. is a very sensitive method for detecting an antigen (see column 1, lines 38-39). It would have been prima facie obvious to use a biotinylated monoclonal antibody and a biotinylated oligonucleotide which form antibody and oligonucleotide complex via streptavidin.

10. Claims 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eberwine et al. (5,922,553, issued Jul. 13, 1999) in view of Eberwine (7,115,371, issued Oct. 3, 2006) and Waggoner (5627027, May 6, 1997) and Sano et al. (5,665,539, issued Sep. 9, 1997) as applied to claims 1-3 and 8-9 above, and further in view of Yamane et al. (6,207,378, issued Mar. 27, 2001).

Yamane et al. disclose a method for easily and effectively amplifying nucleic acid molecules of a single kind (see column 1, lines 65-67). A DNA template comprises a T7 promoter sequence and a T7 terminator sequence (see column 10, lines 20-27). The protein is effectively and easily synthesized from the amplified DNA template (see column 6, lines 19-24).

One of ordinary skill in the art would have been motivated to include a T7 promoter sequence and a T7 terminator sequence in an oligonucleotide as taught by Yamane et al. because of the well known benefit of such sequences (see column 6, lines 19-24). It would have been prima facie obvious to use an oligonucleotide including in a T7 promoter sequence and a T7 terminator sequence.

11. Claims 4-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eberwine et al. (5,922,553, issued Jul. 13, 1999) in view of Eberwine (7115371, issued Oct. 3, 2006) and Waggoner (May 6, 1997) and Sano et al. (5,665,539, issued Sep. 9, 1997) as applied to claims 1-3 and 8-9 above.

None of the references above discloses the size of the double stranded DNA.

However, one of ordinary skill in the art would have been motivated to optimize a reaction condition by optimizing the size of the double stranded DNA with a reasonable expectation of success because it was routine practice in the art to optimize a reaction condition (see M.P.E.P. 2144.05). It would have been prima facie obvious to apply a double stranded oligonucleotide having at least 100 base pairs or 500 base pairs.

Summary

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637

/Joyce Tung/
Examiner, Art Unit 1637
October 09, 2009